

REMARKS/ARGUMENTS

This amendment is filed in response to the Office Communication mailed April 6, 2005. Applicants thank the Examiner for the telephone conversation of April 18, 2005 with Anina Murphy, in which the Office Communication was discussed. Examiner Walicka requested that the changes made in the substitute sequence listing, specifically SEQ ID NO:42, be explained. Applicants identify and describe all of the amended sequences below. Upon review, it was noted that the substitute sequence listing, filed January 27, 2005, improperly presented SEQ ID NO:44. The correction of this error in a second substitute sequence listing is also discussed below.

Sequences Amended in First Substitute Sequence Listing filed January 27, 2005

SEQ ID NO:42

The specification describes SEQ ID NO:42, on page 10, lines 20-24, as a polynucleotide encoding residues 46-501 of human beta-secretase. The polynucleotide would consist of residues 136-1503 of the human beta secretase gene (See, *e.g.*, Figure 1A). As amended in the substitute sequence listing filed January 27, 2005, SEQ ID NO:42 recites residues 136-1503 of the beta secretase gene. SEQ ID NO:42 in the original sequence listing recited 2348 nucleotides.

As SEQ ID NO: 42 is described on page 10, lines 20-24 of the specification as being a polynucleotide encoding the active enzyme form (amino acid residues 46-501) of human beta-secretase, and the nucleotide and amino acid sequences of human beta secretase are disclosed in Figures 1A, and 1B, SEQ ID NO:42 as amended in the substitute sequence listing is not new matter.

SEQ ID NO: 45

SEQ ID NO:45 is identified on page 8, lines 9-11 of the specification, as depicting the underlined sequence of depicted in Figure 3A, DYKDDDDK. This sequence consists of eight amino acid residues. SEQ ID NO:45 was amended in the substitute sequence listing to

conform to that sequence. SEQ ID NO:45 in the original sequence listing consisted of seven amino acid residues, YKDDDDK.

The specification identifies SEQ ID NO:45, on page 8, lines 9-11, as being the underlined sequence of Figure 3A, which is the eight amino acid residue peptide DYKDDDDK. As SEQ ID NO:45 recites that sequence, the amended SEQ ID NO:45 is not new matter.

SEQ ID NO:46

The specification identifies SEQ ID NO:46, on page 8, lines 14-20, as reciting the signal sequence segment of the beta secretase protein. Original Figure 5 identifies the signal sequence segment of beta secretase as consisting of amino acid residues 1-21 of the complete protein. SEQ ID NO:46 was amended in the substitute sequence listing to recite amino acid residues 1-21 of beta secretase. SEQ ID NO:46 in the original sequence listing recited 22 amino acid residues.

Original Figure 5 identifies SEQ ID NO:46 as residues 1-21 of beta secretase. As SEQ ID NO:46 in the substitute sequence listing conforms to the sequence meeting that description, the amended SEQ ID NO:46 is not new matter.

SEQ ID NO:47

The specification identifies SEQ ID NO:47, on page 8, lines 14-20, as reciting the pre pro segment of the beta secretase protein. Original Figure 5 identifies the pre pro segment of beta secretase as consisting of amino acid residues 22-45 of the complete protein. SEQ ID NO:47 was amended in the substitute sequence listing to recite amino acid residues 22-45 of beta secretase. SEQ ID NO:47 in the original sequence listing recited 23 amino acid residues.

Original Figure 5 identifies SEQ ID NO:47 as residues 22-45 of beta secretase. As SEQ ID NO:47 in the substitute sequence listing conforms to the sequence meeting that description, the amended SEQ ID NO:47 is not new matter.

SEQ ID NO:98

Applicants refer to the underlined section of the third paragraph on page 8 of the amendment filed July 13, 2001 regarding SEQ ID NO:98 which states:

The BRIEF DESCRIPTION OF THE DRAWINGS section was replaced with a replacement section which includes the following amendments. SEQ ID NO: 78 was originally used twice to refer to two different sequences. The specification is amended to identify the second of these sequences, first mentioned in Figure 9, as SEQ ID NO: 98. The sequence identifier SEQ ID NO: 80 was added to the description of Figure 14A. Sequence identifiers SEQ ID NO: 103 and SEQ ID NO: 104 were added to the description of Figure 19B to comply with the requirements 37 C.F.R. §1.821.

Figure 9, as amended, identifies SEQ ID NO:98 as a nucleic acid sequence encoding a fragment of beta secretase. This sequence is identified in Figure 9 as CCCGAAGAGCCCGGCCGGAGGGGCAGCTTTGTCGA. SEQ ID NO:98 was amended in the substitute sequence listing to recite that sequence. SEQ ID NO:98 in the original sequence listing recited the sequence CCCGAGGAGCCCGGCCGGAGGGGCAGCTTTGTCGA.

Original Figure 9 identifies SEQ ID NO:98 as CCCGAAGAGCCCGGCCGGAGGGGCAGCTTTGTCGA. As SEQ ID NO:98 in the substitute sequence listing recites the same sequence, the amended SEQ ID NO:98 is not new matter.

Each of the amended sequences described above remains unchanged, i.e., has not been further amended, in the second substitute sequence listing filed herewith.

Second Substitute Sequence Listing Filed Herewith

In responding to Examiner Walicka's comments regarding SEQ ID NO:42, it was noted that the substitute sequence listing, filed January 27, 2005, improperly presented SEQ ID NO:44, which is a polynucleotide (with 5' and 3' untranslated regions) encoding human beta secretase, seen in Figure 1B. SEQ ID NO:44 was properly presented in the original sequence listing filed July 13, 2001. A second substitute sequence listing, is filed herewith in accordance with 37 C.F.R. 1.821-1.825 to properly present SEQ ID NO:44.

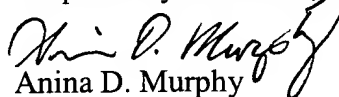
The second substitute sequence listing, presented in both computer readable and paper formats, properly presents all of the sequences of the instant application. The second substitute sequence listing in computer readable format was prepared through the use of the software program "FastSEQ for Windows Version 4.0" and is identical to that of the paper copy of the second substitute sequence listing in the Appendix. The second substitute sequence listing conforms the sequences disclosed to the sequences presented in the specification and figures as originally filed. These amendments contain no new matter.

Amendments to the Specification

Upon review, it was also noted that the paragraph beginning on page 8, line 14, had been altered without formal amendment in the course of prosecution. Specifically, the residues comprising the signal sequence, and the pro region of beta secretase had been changed to conform to the residues disclosed in original Figure 5 without formal amendment. Those sequences are now conformed to Figure 5 by this amendment. All other amendments to that paragraph made in the course of prosecution remain intact. In addition, the same paragraph has been amended to correctly identify the residue at which the transmembrane region of beta secretase commences as being amino acid residue 455. This amendment also conforms the specification to Figure 5 as originally filed. As each of the amendments to the specification conform the paragraph to original Figure 5, they are not new matter.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,


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APPENDIX: Second Substitute Sequence Listing